

CURRICULUM VITAE

NAME: Hyun K. Kim

DATE AND PLACE OF BIRTH: December 27, 1934; Seoul, Korea

CITIZENSHIP: United States of America by Naturalization in June 1972

MARITAL STATUS: Married:
Wife, Youngsook
Daughter, Jane

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EDUCATION:

Undergraduate Education: B.S. 1957, Seoul National University, Seoul, Korea
The University scholar - 1953 - 1957
Graduate education: Ph.D. 1963, University of Michigan, Ann Arbor, Michigan
Thesis advisor: The late Professor Fred F. Blicke
Thesis title: Reactions of Ivanov-like reagents prepared from N,N-disubstituted toluene- α -sulfonamides.
The University scholar - 1959 - 1960
Postdoctoral fellow: June 1963 - July 1965, Vanderbilt University under the direction of Professor Lamar Field in organosulfur chemistry.

BRIEF CHRONOLOGY OF EMPLOYMENT:

1965 - 1966 - Research chemist, E.I. du Pont de Nemours and Co., Parlin, New Jersey.
1966 - 1969 - Organic research chemist, Hess and Clark, Division of Richardson Merrell, Inc.
Ashland, Ohio
1970 - 1971 - Senior research scientist, Bristol Laboratories, Syracuse, New York
1972 - Present - Chemist, Contraception, and Reproductive Health Branch, Center for Population Research,
National Institute of Child Health and Human Development, National Institutes of
Health, Bethesda, Maryland

RESEARCH INTERESTS:

E.I. du Pont de Nemours and Company - Synthesis and application of new organosulfur sensitizers and stabilizers for X-ray film and others.

Hess and Clark, Division of Richardson Merrell, Inc., - Synthesis of nitroheterocyclic nitrones and their 1,3-dipolar cycloaddition products as orally active **antibacterial**, antiprotozoal, anthelmintic and growth promoting agents for domestic animals - A facile cope type rearrangement. Radiolabelled synthesis of nifuratrone with carbon-14.

Bristol Laboratories: Total Synthesis of 13-ethyl Ring B-thia steroids as antifertility agents. Synthesis of tricyclic heterocycles as cardiovascular drugs and antisecretory agents.

National Institutes of Health: Contraception and reproductive health branch, Center for population research, National Institute of Child Health and Human Development: Participate as a Project Officer for synthetic contracts directed to development of chemical contraceptives and reproductive health drugs in monitoring the performance of R&D from both the scientific and management view points. Directly interacted with the contractors and guided them whenever problems in the synthesis of chemical contraceptives and reproductive health drugs have occurred. It involves the area of drug design using computer-aided 3D-modeling using Insight II, Quanta/Charmm and Sybyl software, syntheses and molecular modification for structure activity relationships using Comparative Field Analysis (CoMFA), and docking with the receptor and ligand. Responsible for the supervision of the maintenance and operation of the synthetic chemical facility and synthetic peptide facility for the Contraception and Reproductive Health Branch. Determine the best routes of syntheses for drugs, chemicals, and other intermediates, and assign priorities for work to be quickly accomplished. Design new lead contraceptives and reproductive health drugs using 3D-QSAR, CoMFA (Comparative Field Analysis) and Insight II. Was responsible for bulk production (2 kg) of 17 α -acetoxy-11 β -(4-N,N-dimethylaminophenyl)-19-norpregna-4,9-diene-3,20-dione (CDB-2914) via multistep syntheses under cGMP conditions for clinical trials. Participate with staff of the Branch, the Center, and the Institute in the management and execution of a contraceptive and reproductive health drug development program both in male and female.

PUBLICATIONS AND PATENTS:

(See attached bibliography)

Author or co-author of 33 publications and holder of 7 U.S. patents and 1 foreign patents.

PROFESSIONAL ASSOCIATION AND HONORS:

Member, American Chemical Society

Member, The Society of Sigma Xi

Member, The American Institute of Chemists

AWARDS:

1. 1984: 10 years Service Award as an employee of the Government of the United States of America.
2. October 1992: 20 years Service Award as an employee of the Government of the United States of America.

BIBLIOGRAPHY

1. Organic Disulfides and Related Substances. XV. Attempted synthesis of mercapto disulfides; L. Field and H.K. Kim. 1966 *J. Org. Chem.*, **31**, 597 - 599.
2. Organic Disulfides and Related Substances. XVII. Analogs of o-(2-aminoethyldithio)benzoic acid as antiradiation drugs; L. Field and H.K. Kim 1966 *J. Med. Chem.*, **9**, 397 - 402.
3. Organic Disulfides and Related Substances. XXI. Sulfur chloride in the preparation of thiosulfonates from disulfides; J.D. Buckman, M. Bellas, H.K. Kim. 1967 *J. Org. Chem.*, **32**, 1626 - 1627.
4. Organic Disulfides and Related Substances. XXIV. Unsymmetrical n-decylaminoethyl disulfides as antiradiation drugs; L. Field, H.K. Kim and M. Bellas 1967 *J. Med. Chem.*, **10**, 1166-1167.
5. Nitrones. I. α -(5-Nitro-2-furyl)-N-arylnitrones; H.K. Kim and R.E. Bambury 1969 *J. Med. Chem.*, **12**, 719 - 720.
6. Nitrones. II. α -(5-Nitro-2-furyl)-N-cycloalkyl- and N-alkylnitrones; H.K. Kim, H.K. Yaktin and, R.E. Bambury 1970 *J. Med. Chem.*, **13**, 238 - 241.
7. Nitrones. III. α -(5-Nitro-2-furyl)-N-hydroxyalkylnitrones and their derivatives; H.K. Kim, R.E. Bambury and H.K. Yaktin. 1971 *J. Med. Chem.*, **14**, 301 - 304.
8. Nitrones. IV. A Facile Cope-Type reaction; H.K. Kim and P.M. Weintraub. 1970 *J. Org. Chem.*, **35**, 4282 - 4283.
9. Nitrones. V. Vinyllogs of α -(5-Nitro-2-heteroaryl)-N-substituted Nitrones; H.K. Kim and R.E. Bambury. 1971 *J. Med. Chem.*, **14**, 366 - 367.
10. Nitrones. VI. α -(5-Nitroimidazol-2-yl)-N-substituted Nitrones; R.E. Bambury, C.M. Lutz, L.F. Miller, H.K. Kim and H.W. Ritter 1973 *J. Med. Chem.*, **16**, 566 - 568.
11. Formyl Substituted Phenazine 5,10-Dioxides; M.L. Edwards, R.E. Bambury and H.K. Kim 1976

- J. Heterocyclic Chem.*, **13**, 653 - 656.
12. Nitrones. VII. α -Quinoxaliny-N-substituted Nitroene 1,4-dioxides; H.K. Kim, L.F. Miller, R.E. Bambury and H.W. Ritter. 1977 *J. Med. Chem.*, **20**, 557 - 560.
 13. Synthesis of 11 α - and 11 β -Diethylaminoethyl ethers of 17 α -Ethinylestradiol; C.M. DiNunno, P.N. Rao and H.K. Kim. 1981 *J. Chem. Soc. Perkin Trans I*, 2401 - 2404.
 14. Synthesis of 17 α -Ethinyl-7 α ,11 β -dihydroxyestra-1,3,5(10)-trien-3,17-diol; J.E. Burdett, Jr., P.N. Rao, H.K. Kim, M.J. Karten and R.P. Blye 1982 *J. Chem. Soc. Trans I*, 2877 - 2880.
 15. 7 α -Methylnorethindrone enanthate 10 β -Hydroperoxide: Isolation and Characterization; C.M. DiNunno, J.E. Burdett, Jr., P.N. Rao, H.K. Kim and R.P. Blye 1983 *Steroids*, **42**, 401 - 408.
 16. Development and Use of a Radioimmunoassay for D-(-)-Norgestrel 17 β -Cyclopentanecarboxylate; R.P. Blye, H.K. Kim, M.C. Lindberg, S.B. Mitra, R.H. Naqvi, D.M. Peterson and P.N. Rao. 1986 *Steroids*, **48**, 27 - 45.
 17. Synthesis of 3-(3-pyridyl) and 3-(3-benzo[b]thienyl)-D-alanine; P.N. Rao, J.E. Burdett, Jr., J.W. Cessac, C.M. DiNunno, D.M. Peterson and H.K. Kim. 1987 *Int. J. Peptide Protein Res.* **29**, 118 - 125.
 18. An improved pinacol rearrangement for the synthesis of 2-alkyl-1,3-cyclopentanediones; R.A. Martinez, P.N. Rao and H.K. Kim. 1989 *Synth. Commun.* **19**, 373 - 377.
 19. Tritium labelled *trans*-4-n-butyl-2,3-³H-cyclohexanecarboxylic acid. Preparation of testosterone 17 β -*trans*-4-n-butyl-2,3-³H-cyclohexanecarboxylate and [4-¹⁴C]-testosterone 17 β -*trans*-4-n-butylcyclohexanecarboxylate; C.K. Acosta, J.W. Cessac, P.N. Rao and H.K. Kim. 1990 *J. Label. Compound Radiopharm.*, **28**, 1201 - 1212.
 20. Synthesis of α -BOC-*trans*-4-Aminocycloalkyl-D-alanine and α -BOC-*cis*-4-Aminocycloalkyl-D-alanine; P.N. Rao, D.M. Peterson, C.K. Acosta, M.L. Bahr and H.K. Kim. 1991 *Org. Prep. Proced. Int.*, **23**, 103 - 110.
 21. Synthesis of Unnatural Amino Acids; C.K. Acosta, M.L. Bahr, J.E. Burdett, Jr., J.W. Cessac, R.A. Martinez, P.N. Rao and H.K. Kim. 1991 *J. Chem. Research (S)*, 110 - 111.
 22. Chirospecific Synthesis of D and L-p-Chlorobomophenylalanine-N-t-BOC DCHA (Dicyclohexylamine) Salt; J.W. Cessac, P.N. Rao and H.K. Kim. 1993 *J. Amino Acids*, **6**, 97 - 105.
 23. Tetrapropylammonium Perruthenate (TPAP) As a Mild and Efficient Oxidant For Sensitive Steroidal Alcohols; C.K. Acosta, P.N. Rao and H.K. Kim. 1993 *Steroids*, **58**, 205 - 208.
 24. Preparative Chemical Methods for Aromatization of 19-Nor- Δ^4 -3-oxosteroids; P.N. Rao, J.W.

- Cessac and H.K. Kim. 1994 *Steroids*, **59**, 621 - 627.
25. Synthesis of New Immunogens for the development of Radioimmunoassay of Levonorgestrel and its 3-oximes; P.N. Rao, C.K. Acosta, D.M. Peterson and H.K. Kim. 1994 *J. Ind Inst. Sci.*, Jan.-Feb. **74**, 35 - 50.
 26. Oxidative Demethylation of 4-Substituted N,N-Dimethylanilines with iodine and calcium oxide in the presence of methanol; C. K. Acosta, J.W. Cessac, P.N. Rao and H.K. Kim. 1994 *J. Chem. Soc. Chem. Commun.*, 1985.
 27. Studies on the Stability of (\pm)-Gossypol, (\pm)-Gossypol Acetic Acid and (+)-Gossypol; N. Bunyapraphatsara, S. Kasnick, A.T. Elvin, G.A. Cordell, H.H.S. Fong, S.A. Matlin, Z.-R. Hua, S. Roshdy, H.K. Kim, P.N. Rao, W.-M. Zhou, L.-B. Long, W.-J. Shen and H. Liang. 1994 *Thai. J. Phytopharmacy* **1**, 1 - 9.
 28. Steroid Specificity of the Human Sperm Progesterone Receptor; N.J. Alexander, H.K. Kim, R.R. Blye and P.F. Blackmore. 1996 *Steroids*, **61**, 116 - 125.
 29. 11 β -Substituted 13 β -ethyl gonane derivatives exhibit reversal of antiprogestational activity: P.N. Rao, J.W. Cessac, R.P. Blye and H.K. Kim (1998) *Steroids*, **63**, 50- 57 .
 30. Synthesis of N-Demethylated Derivatives of 17 β -Acetoxy-11 β -(4-N,N-Dimethylaminophenyl)-19-Norpregna-4,9-diene-3,20-dione and mifepristone. Substrates for the Synthesis of Radioligands. (1999) P.N. Rao, C.K. Acosta, J.W. Cessac, M.L. Bahr and H.K. Kim *Steroids*, **64**, 205 - 212.
 31. A Practical Large Scale Synthesis of 17 α -Acetoxy-11 β -[4-(N,N-Dimethylamino)phenyl]-19-Norpregna-4,9-Diene-3,20-Dione (CDB-2914) (2000) Rao PN, Acosta CK, Martin LB, Burdett JE, Cessac JW, Morrison PA and Kim, HK *Steroids*, **65**, 395 - .
 32. Synthesis of 11 β -Hydroxy-D-norgestrel 11-Nitrate ester; C.K. Acosta, P.N. Rao and H.K. Kim
This paper was presented at 9th International Congress on Hormonal Steroids in Dallas, Texas
September 24 - 29, 1994.

U.S. Patents

1. R.E. Bambury and H.K. Kim, "Cycloalkyl Nitrofurylnitrones" : U.S. 3,528,971 (1970).
2. R.E. Bambury and H.K. Kim, " α -(5-Nitroimidazol-2-yl)-N-substituted Nitrones" : U.S. 3,583,985 (1971).
3. H.K. Kim, "1,4-Dioxidoquinoxaliny Nitrones": U.S. 3,644,363 (1974).
4. R.P. Blye and H.K. Kim, "7 α -Methylnorethindrone enanthate and its use in long term suppression of fertility in female mammals": U.S. 4,252,800 (1981).
5. S. Archer, G. Bialy, R.P. Blye, P. Crabbe, E.R. Diczfalusy, C. Djerassi, J. Fried and H.K. Kim, "Long-Acting Androgenic Compounds and Pharmaceuticals Thereof": U.S. Patent 4,948,790: Issued, August 14, 1990.
6. G. Bialy, R.P. Blye and H.K. Kim, "Orally active derivatives of 1,3,5(10)-estratriene": U.S. Patent 5,554,603: Issued, Sept. 10, 1996.
7. H.K. Kim, P.N. Rao, J.E. Burdett, Jr., C.K. Acosta, "Method for preparing 17 α -Acetoxy-11 β -(4-N,N-dimethylaminophenyl)-19-norpregna-4,9-diene-3,20-dione, intermediates useful in the method, and methods for the preparation of such intermediates": U.S. 5,929,262: Issued, July 27, 1999
8. H.K. Kim, R.P. Blye, P.N. Rao, J.W. Cessac and C.K. Acosta, "21-Substituted progesterone derivatives as new antiprogestational agents": U.S. Patent Application Serial No. 60/016628; Filing Date, 5/01/1996.
9. HK Kim, C.K. Acosta, RP Blye, JW Cessace, AM Simmons, and PN Rao, Structural Modifications of 19-norprogesterone derivatives I: 17 α -substituted, 11 β -4-substituted aryl and 21-substituted 19-norpregnadienedione derivatives as new antiprogestational agents. U.S. Patent Application Serial No. 09/180,132, filed May 24, 1999; PCT/US97/07373, filed April 30, 1997; and 60/016,628, filed May 1, 1996, CIP Filing Date, March 17, 2000.
10. HK Kim, PN Rao, JW Cessac, AM Simmons, Improved Process Development of 17 α -acetoxy-11 β -4-(N,N-dimethylamino)phenyl]-21-methoxy-19-norpregna-4,9-diene-3,20-dione and intermediates useful in methods for the preparation of the same. U.S. Provisional Patent Application Serial No. 60/173,470; Filing Date, Dec. 29, 1999
11. R.P. Blye and H.K. Kim Method of Making and Using 7 α , 11 β -Dimethyl-17 β -hydroxy-4-estren-3-one 17 β -trans-4-n-butylcyclohexanecarboxylate and 17 β -undecanoate. U.S. Provisional Application Serial No. 60/194,440 ; Filing Date, April 4, 2000

Foreign Patent:

1. R.E. Bambury and H.K. Kim, "N-Substituted Nitrofuryl Nitrones": Belgium Patent No. 720702 (1969)
2. Orally active derivatives of 1,3,5(10)-estratriene: Submitted foreign patent application to the International Bureau of the Patent Corporation Treaty on February 21, 1994.
3. Method for preparing 17 α -Acetoxy-11 β -(4-N,N-dimethylaminophenyl)-19-norpregna-4,9-diene-3,20-dione, intermediates useful in the method, and methods for the preparation of such intermediates" Submitted foreign patent application to the International Bureau of the Patent Corporation Treaty. International application No. PCT/US96/03660: International filing date, March 18, 1996
4. H.K. Kim, R.P. Blye, P.N. Rao, J.W. Cessac and C.K. Acosta, "21-Substituted progesterone derivatives as new antiprogestational agents": International application No. PCT/US/97/07373: International filing date: April 30, 1997.